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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/713,572	11/15/2000	Kenneth A Giuliano	97.022-K2	5670
20306	7590	06/17/2005	EXAMINER	
MCDONNELL BOEHNEN HULBERT & BERGHOFF LLP 300 S. WACKER DRIVE 32ND FLOOR CHICAGO, IL 60606			WALICKA, MALGORZATA A	
			ART UNIT	PAPER NUMBER
			1652	

DATE MAILED: 06/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/713,572

Applicant(s)

GIULIANO ET AL.

Examiner

Malgorzata A. Walicka

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 03 March 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 10-17 and 24-31 is/are pending in the application.
- 4a) Of the above claim(s) 17 and 24-31 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-16 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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Response to Restriction Requirement filed March 03, 2005 is acknowledged. Claims 10-17 and 24-31 are pending. Elected claims 10, 13-16 reading on the elected invention, a 3-domain biosensor comprising elected species SEQ ID NO: 44, 118 and 150 are under examination. Claims 10-16, 17 and 24-31 directed to other species and inventions are withdrawn from examiner's consideration as being drawn to the non-elected invention; see 37 CFR 1.142(b).

Detailed Action

1. Restriction/election

Applicant's election, with traverse, of Group I, claim 10, 13, 14, 15, 16, 17 in part, drawn to a 3-domain biosensor comprising detectable polypeptide signal, protease recognition site and reactant target sequence set forth by of SEQ ID NO: 43, 117 and 149, classified in class 530, subclass 387.3 is acknowledged. It is understood for the nature of the instant invention that the species of SEQ ID NO: 43, 117 and 149 that identify nucleotide sequences should be SEQ ID NO: 44, 118 and 150 that identify amino acid sequences.

The traversal is on the ground(s) that the search required for Group I is also required for Groups II and III and Applicants note the presently pending claims were restricted out as a single inventive group in the parent case to which this application claims priority.

Applicants' arguments have been fully considered, but are found not persuasive for the reasons explained in the restriction requirement. Biosensors of Group I-III are different chemical compounds, having different chemical structure,

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although they may contain the same domains. Thus they are different products. It is unclear to the examiner which parental application the Applicants are referring to in their traversal. The only utility application to which the priority is claimed is US application 09/430/656. This application, however, does not disclose the subject matter of the instant claims. In summary, the restriction as requested, is proper and made FINAL. Elected claims 10, 13-17 in part directed to a 3-domain biosensor comprising SEQ ID NO: 44, 118 and 150 are under examination. Claims 10-17 and 24-31 directed to other species and inventions are withdrawn from examiner's consideration as being drawn to the non-elected invention; see 37 CFR 1.142(b).

2. Objections

2.1. Priority

Applicants claim of priority to the provisional applications 60/136,078, filed May 26, 1999 and 60/106,308 filed October 30, 1998 is acknowledged. The priority to the provisional applications is granted. However, the priority to US applications 09/430,656 filed October 29, 1999, 08/031,271 filed according to Applicants Feb. 27, 1998 and to application 08/810,983 (patent 5, 989,835) filed Feb. 29, 1997 is not granted because these application do not disclose the subject matter claimed in the instant application. The application 08/031,271 filed according to Applicants Feb. 27, 1998 is filed by others in 1993 and entitled "Automatically latched safety syringe". The application 08/810,983 (patent 5, 989,835) filed Feb.9, 1997 is by the other inventive entity (Terry D. and

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Lansing T.). Please correct the priority claim by providing a new oath and amending the specification.

2.2. The specification

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors in the specification of which applicant may become aware.

3. Rejections

3.1. *35 USC § 112, second paragraph*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claim 10 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The language of the claim is confusing in part b. The phrase "a second domain comprising at least protease recognition site" is unclear. For examination purposes the examiner assumes that the correct phrase is "comprising a protease recognition site".

3.1. **35 USC § 112, first paragraph**

The following is a quotation of the first paragraph of 35 U.S.C. 112:

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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3.1.1. Written description

Claims 10 and 13-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are directed to a recombinant protease biosensor comprising at least one detectable polypeptide signal, a protease recognition site and at least one reactant target sequence. The claims are suffering from lack of written description of structure and function.

Regarding claim 10 it is unknown what is the exacted function, i.e., which protease is sensed, how many detectable polypeptide signals and reactant sequences are used to construct the biosensor, what their structures are and what is the entire structure. The signal polypeptides, protease recognition site and reactant target sequences are comprised in one bigger structure. The structure of linkers and flanking sequences should be identified. The full structure of a biosensor comprising elected species of three domains, i.e., SEQ ID NOs: 44, 118 and 150 is not disclosed, neither it is demonstrated that any of such biosensors is recognized by neurotoxin E protease.

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Applicants teach many species of full structure of a three domain biosensor and they are listed in the sequence listing or in claim 17. These structures, however, are not representatives of all protease biosensors broadly claimed by Applicants. The full structure of a biosensor comprising elected species of three domains, i.e., SEQ ID NOs: 44, 118 and 150 is not disclosed. Applicants attention is turned to the fact that reciting in the examined claims nine signal domains, thirty five protease recognition sites and sixteen target sequence domains does not provide identifying structure of all claimed genus of biosensors, but only representative species of three subgenera of the domains used for their construction. The recited sequences even do not identify the subgenera of respective domains because the subgenera of signal domains, protease recognition sites and reactant target domains are large and versatile. There are other signal domains, protease recognition sites and reactant target domains that can be components of biosensors encompassed by the scope of the claims.

In conclusion, because the claims are lacking sufficient written description of structure and function of the claimed biosensors, one skilled in the art is not convinced that Applicants were in possession of the claimed invention at the time the application was filed.

3.1.2. Scope of enablement

Claim 10 and 13 -16 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for elected species of domains of SEQ ID NO: 44,

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118 and 150, or a full structure of many biosensors none of which contains SEQ ID NO: 44, 118, and 150, does not reasonably provide enablement for:

- 1) any protease biosensor as claimed by claim 10,
- 2) any protease biosensor having as a polypeptide signal any protein encompassed by claim 13,
- 3) any protease biosensor wherein polypeptide signal domain comprises sequences recited by claim 14,
- 4) any protease biosensor wherein protease recognition site is any of sequences recited in claim 15, and
- 5) any protease biosensor wherein the reactant target sequence domain comprises a sequence listed in claim 16.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Otherwise, undue experimentation is necessary to make the claimed invention.

Factors to be considered in determining whether undue experimentation is required are summarized *In re Wands* [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill

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of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breath of the claimed invention encompasses any three domain protease biosensor which

- 1) is protease biosensor as claimed by claim 10, wherein all domains originate for any natural or man-made source;
- 2) is protease biosensor having as a polypeptide signal any protein encompassed by claim 13;
- 3) is any protease biosensor wherein polypeptide signal domain comprises sequences recited by claim 14;
- 4) is protease biosensor wherein protease recognition site is any of sequences recited in claim 15, and
- 5) is protease biosensor wherein the reactant target sequence domain comprises a sequence listed in claim 16.

While methods of constructing chimeric proteins comprising any of the component of the claimed biosensor are well known in the relevant art, and skills of the artisans highly developed, to make any biosensor as listed under 1)-5) above is out of routine experimentation because lack of instruction as to how to connect the three domains to obtain the biosensor that possesses the desired function, i.e., works as intended. Applicants own data indicates that even if the structure of a biosensor is known in its entirety, the function may be other than intended. On page 100 Applicants

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teach the construction of biosensor of SEQ ID NO: 2 which is **caspase-3** biosensor.

However, on page 102, two last lines, and further on page 103, Applicants state,

"This also implies that the current **biosensor, although designated to be caspase 3-specific**, is indeed specific for a class of caspases rather than uniquely specific for caspase-3. **The 'most likely candidate is caspase-7** [emphasis added]."

This passage obviously indicate that the function of the protease biosensor may be different than intended, and unless it is proved by Applicant what function is connected with the specific structure of the protease biosensor, i.e., without explicitly stating the exact structure and function of the protease biosensor one skilled in the art is forced to extensive experimentation with a low probability of success in obtaining the claimed invention.

Examiner concludes that without a further detailed guidance on the part of Applicants regarding the structure of the claimed protease biosensors and their particular function, experimentation left to those skilled in the art is improperly extensive and undue.

4. Conclusion

All claims are rejected.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka whose telephone number is (571) 272-0944. The examiner can normally be reached on Monday-Friday from 10:00 a.m. to 4:30 p.m.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Malgorzata A. Walicka, Ph.D.

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Patent Examiner



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